

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Body mass, cardiovascular risk and metabolic characteristics of young persons presenting for mental health care in Sydney, Australia
AUTHORS	Scott, Elizabeth ; Hermens, Daniel; White, Django; Naismith, Sharon; Gehue, Jeanne; Whitwell, Bradley; Glozier, Nick; Hickie, Ian

VERSION 1 - REVIEW

REVIEWER	Cenk Tek Associate Professor of Psychiatry Director, Psychosis Program Yale University Department of Psychiatry and Connecticut Mental Health Center Connecticut, USA
REVIEW RETURNED	30-Dec-2014

GENERAL COMMENTS	<p>Chronic mental illness kills. Mostly because of ailments that kills everybody else, alas much younger. The excess morbidity and early mortality is mostly associated with obesity related illnesses. We have previously have shown that patients who enroll in first episode services have comparable metabolic profiles to their community peers but about double their cardiovascular risk in the first year. We have defined this period as the critical period to develop interventions to develop prevention programs to prevent excess morbidity and early mortality decades later. (Schizophr Res. 2013 May;146(1-3):64-8. doi: 10.1016/j.schres.2013.01.014. Epub 2013 Feb 17.</p> <p>Cardiovascular mortality in schizophrenia: defining a critical period for prevention. Srihari VH1, Phutane VH, Ozkan B, Chwastiak L, Ratliff JC, Woods SW, Tek C.). Notably this paper is not cited but I assume the authors are aware of the findings. i do strongly urge the use of Max Birchwood's critical period concept which served us well for stimulating psychiatric early interventions for psychosis. Clearly more data to support the concept is necessary which will in turn will stimulate holistic early intervention services.</p> <p>The study takes advantage of the wonderful Australian experiment Headspace's data to give us a snapshot of the rough metabolic profile of people with some kind of mental illness before the mental illness becomes chronic. Good news is they are similar to the rest of population (although one third are overweight and obese which is sign of the sad state of affairs about obesity and population). Smoking rates were higher in the probands. The combination of higher weight and higher rates of smoking potentially explains higher future cardiovascular and metabolic risk without hinting at causality,</p>
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	<p>but at least rules out an innate increased cardiovascular risk for young people presenting with some kind of mental distress. For a clinician and researcher such as myself, working in the area, this snapshot is useful. I do hope the authors follow this up with the point where the break from non-ill peer occurs, to define this critical period better, at least for these Western developed country populations.</p> <p>I would not give much heed to the lack of relationship between high fasting glucose and excess body weight in this sample, since it takes many years for insulin resistance and diabetes to develop, hence our opportunity to intervene. On the other hand, the changes in adiposity is hinted with changing blood lipid profiles, which essentially may mean the critical period is short and rapid development and dissemination of interventions is sorely needed.</p> <p>The paper is straightforward, sample size is large, findings are useful. Nothing is found dramatically new, but confirmation of existing knowledge with a large enough sample is important for me. I thank the authors for their effort.</p>
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REVIEWER	Dr Evan Atlantis University of Western Sydney, Australia
REVIEW RETURNED	02-Feb-2015

GENERAL COMMENTS	<p>The submitted manuscript reports findings from a cross-sectional study on the presence of cardiovascular risk actors among a varying sample of young people presenting for mental health care in Sydney, Australia.</p> <p>The investigators reported several associations, and their conclusions focused on high levels of smoking, and association of BMI with adverse social circumstances.</p> <p>I congratulate the authors for generating such an interesting study and well-written paper, contributing important new information in the field.</p> <p>I present several suggestions for improvement, for their discretionary consideration.</p> <p>Abstract: Table 1b shows associations of BMI category and HDL and triglycerides, which was omitted, perhaps not balanced. The conclusion should correct the study population, as 'young people presenting for mental health care'. The statement on future risk is too speculative and not supported by the study's cross-sectional data, especially for the abstract.</p> <p>Key messages: Replace increased 'risks to' with 'risks of'. Replace 'signal' with 'evidence' or 'effect'. Reword the last point along the following: 'is required to prevent the onset of metabolic or cardiovascular disorders.'</p> <p>Results: Avoid using 'cohort' in observational research, which has a different meaning than 'group' (i.e. prospective or retrospective cohort study).</p> <p>Discussion: The proposition that there was no or little evidence supporting</p>
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	<p>assumptions about weight gain and lifestyle risk factors explaining the increased risk of cardio-metabolic disorders among people with mental health problems is a misinterpretation of the study results, in my view. Table 1b shows associations of BMI category and HDL and triglycerides were present in the young population; and there was a very high prevalence of smoking in the population, which is an important lifestyle risk factor for metabolic disorder, especially raised triglycerides.</p> <p>The early stage of life in the study population and chronic nature and delayed onset of disease likely explains the weak associations and 'relatively normal' results.</p> <p>The limitations of the study could have been better acknowledged, including healthy group seeking care and selection biases, i.e. results may not be relevant to other young people with mental health problems, and other settings/countries.</p> <p>I hope my comments are helpful.</p>
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VERSION 1 – AUTHOR RESPONSE

Response to Reviewer 1 [Prof. Cenk Tek]

1.1: The title should give the location of the study as should the abstract.

1.1-Reply: We have amended the title and abstract as follows:

New title: 'Body mass, cardiovascular risk and metabolic characteristics of young persons presenting for mental health care in Sydney, Australia'

The relevant sentence in the Abstract is now:

'Setting: Two primary-care based sites in Sydney, Australia for young people in the early stages of mental disorders'.

1.2: We have previously have shown that patients who enrol in first episode services have comparable metabolic profiles to their community peers but about double their cardiovascular risk in the first year. We have defined this period as the critical period to develop interventions to develop prevention programs to prevent excess morbidity and early mortality decades later. (Schizophr Res. 2013 May;146(1-3):64-8. doi: 10.1016/j.schres.2013.01.014. Epub 2013 Feb 17.

Cardiovascular mortality in schizophrenia: defining a critical period for prevention.

Srihari VH1, Phutane VH, Ozkan B, Chwastiak L, Ratliff JC, Woods SW, Tek C.). Notably this paper is not cited but I assume the authors are aware of the findings.

1.2-Reply: We agree that this is an important finding to cite and thus we have added/re-written the following text to the Discussion (see last paragraph):

"Of note, a US study of 76 young, first episode psychosis (schizophrenia) patients attending an urban community mental health centre were found, at entry, to have comparable metabolic profiles to their community peers [Srihari et al. 2013]. However, over the course of the subsequent year, these patients had a significant worsening of cardiovascular risk factors (especially, smoking and obesity). In much of the early psychosis literature, the first year following onset has been described as the 'critical period' [Srihari et al. 2013; Birchwood et al. 1998; McGorry et al. 2008] for the delivery of optimal interventions to prevent excess morbidity and early mortality. This concept has not been extended to include improved physical as well as mental health and other functional outcomes. More recently, there have been major refinements to the concepts of prodromal and critical periods for early psychosis to include the more elaborated notion of clinical staging, thereby capturing a greater continuum of the journey from early symptoms to established illness [McGorry et al. 2006] Further, the concept has been broadened to include young people with emerging mood disorders [McGorry et al. 2014; Scott et al. 2013]. Within this framework, the greatest opportunities for modifying

the course of illness, including physical health comorbidity, are extended to include a wider spectrum of earlier periods of disabling symptoms and the more obvious early periods of discrete disorder. A priority for early intervention research now is to evaluate whether group or individual-level interventions at these very early stages may help to reduce smoking rates or prevent the increased rates of being overweight or obese or of other specific metabolic complications that are common in those young people presenting for specialist mental health care”.

1.3: I do strongly urge the use of Max Birchwood's critical period concept which served us well for stimulating psychiatric early interventions for psychosis. Clearly more data to support the concept is necessary which will in turn will stimulate holistic early intervention services.

1.3-Reply: We agree. This citation has also been included (see 1.2-Reply, above). However, we have also added the more elaborated notion of clinical staging which covers the continuum from early symptom development and early stages of discrete disorder.

Response to Reviewer 2 (Dr Evan Atlantis)

2.1: Abstract: Table 1b shows associations of BMI category and HDL and triglycerides, which was omitted, perhaps not balanced.

2.1-Reply: To address this we have added the following text to the Abstract: “... but significant relationships with triglycerides and HDL were noted”.

2.2: Abstract: The conclusion should correct the study population, as ‘young people presenting for mental health care’.

2.2-Reply: We have corrected this statement in the Abstract as recommended by the Reviewer.

2.3: Abstract: The statement on future risk is too speculative and not supported by the study’s cross-sectional data, especially for the abstract.

2.3-Reply: we have removed the word “future” from the Abstract.

2.4: Key messages: Replace increased ‘risks to’ with ‘risks of’; Replace ‘signal’ with ‘evidence’ or ‘effect’; Reword the last point along the following: ‘is required to prevent the onset of metabolic or cardiovascular disorders.’

2.4-Reply: We have corrected each of these points in the Key Messages section as suggested by the Reviewer.

2.5: Results: Avoid using ‘cohort’ in observational research, which has a different meaning than ‘group’ (i.e. prospective or retrospective cohort study).

2.5-Reply: We have changed the term ‘cohort’ (when referring to the patients in this study) to ‘sample’ throughout the manuscript.

2.6: Discussion: The proposition that there was no or little evidence supporting assumptions about weight gain and lifestyle risk factors explaining the increased risk of cardio-metabolic disorders among people with mental health problems is a misinterpretation of the study results, in my view. Table 1b shows associations of BMI category and HDL and triglycerides were present in the young population; and there was a very high prevalence of smoking in the population, which is an important lifestyle risk factor for metabolic disorder, especially raised triglycerides.

2.6-Reply: In our view, the assessor has misinterpreted our view – so we have sought to explain our interpretation more clearly. In essence, we are in agreement with the assessor with regards to the central importance of increased smoking rates contributing (directly or indirectly) to the increased later rates of coronary heart disease and other poor physical health outcomes. Our emphasis here is on the opportunity within these novel service settings to prevent the rapid movement to being overweight or developing other metabolic changes before they are well established and to specifically intervene to reduce smoking rates. Our point is simply that at this early stage of illness course, that only increased smoking rates are well established.

The second factor with regards to the relationship between increased weight and HDL (but not LDL) and triglyceride changes being evident in Table 1B has now been specifically highlighted, as follows (see Results, page 15):

“As shown in Table 1b, there were significant differences among the BMI categories for triglycerides

and HDL, but no differences in the glucose or LDL levels. Compared to the other two groups, the overweight/obese group had the highest levels of the triglycerides and the lowest levels of HDL”.

Furthermore, we have also added to the Discussion (first paragraph, page 17):

“However, we did find a pattern of high triglycerides and low HDL levels in those who were overweight/obese, which is typically observed in this group”.

2.7: The early stage of life in the study population and chronic nature and delayed onset of disease likely explains the weak associations and ‘relatively normal’ results.

2.7-Reply: We take the Reviewer’s point here and have added/edited the following text (see Discussion, page 19):

“This suggests that younger age and/or earlier stages of illness are likely to be key factors underlying such patterns. However, there is evidence of metabolic abnormalities and increased cardiovascular risk in young people with first episode psychotic attending early intervention or other specialised mental health services...”

2.8: The limitations of the study could have been better acknowledged, including healthy group seeking care and selection biases, i.e. results may not be relevant to other young people with mental health problems, and other settings/countries.

2.8-Reply: The following text has been added to the Discussion (see page 18-19):

“Other limitations of the present study include: (i) a lack of a comparison group (e.g. healthy individuals seeking care); (ii) potential selection biases (e.g. differences in those who decided to under go blood tests versus those that did not); (iii) generalisability (e.g. these results may not be relevant to young people with mental health problems in other settings and/or countries). Future studies should aim to address these issues”.

VERSION 2 – REVIEW

REVIEWER	Evan Atlantis University of Western Sydney, AUSTRALIA
REVIEW RETURNED	01-Mar-2015

GENERAL COMMENTS	The authors adequately addressed my points.
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